

REMARKS

The FTIR peaks at 1711 for Form U at Page 11 in the specification is a typographical error, and should be 1701. Support for the peak at 1701 instead of 1711 is found in Figure 31. Accordingly no new matter has been added.

Claims 1-55 are pending. Claims 10 and 11 are allowed. Claims 1-4, 6, 7, 9, 12-21, 23-27, 29-34, 36-39 and 41-55 are rejected. Claims 5, 8, 22, 28, 35 and 40 are objected to. Claims 2, 9, 14, 19 and 21 are amended. No new matter is added.

Claim rejections - 35 U.S.C. § 112

Claims 4, 6, 7, 9, 15, 16, 19, 20-21, 23, 27, 29, 34 and 39 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctively claim the subject matter which applicant regards as the invention for the reasons set forth at page 2 of the Office Action. Applicants respectfully traverse.

Determining whether a claim is definite requires an analysis of whether one skilled in the art would understand the bounds of the claim when read in light of the specification. *Solomon v. Kimberly-Clark Corp.* 216 F.3d 1372, 55 U.S.P.Q.2d 1279 (Fed. Cir. 2000). If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more. *Id.* Breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689 (C.C.P.A. 1971); M.P.E.P. § 2173.04. If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. § 112, second paragraph. *Id.*

The Office Action alleges that the phrase “contacting a nateglinide in the solid state” in claims 4 and 34 is indefinite because it is not clear what is the polymorph required. The term “solid state” in claims 4 and 34 is used to indicate that there is no particular form of nateglinide required to yield the desired polymorph. As commonly understood by those of skill in the art, “solid” encompasses both crystalline and amorphous forms:

Solid (1) A substance of definite shape, and relatively great density, low internal enthalpy, and great cohesion of its molecules. It may be homogeneous (as crystals and solid solutions) or heterogeneous (as amorphous and colloidal substances).

(emphases added). *Grant & Hackh's Chemical Dictionary*, 5th ed, 1987. The specification also states "the starting material used for the processes of the present invention may be any crystalline or amorphous form of nateglinide, including various solvates and hydrates." *Application*, p. 21, ll. 8-10. Therefore, based on the knowledge of those of skill in the art, and further clarification from the specification, it is clear that nateglinide "in solid state" refers to all forms, including crystalline and amorphous. Because the scope of the subject matter embraced by claims 4 and 34 is clear, breadth of these claims is not indefiniteness, and the claims comply with 35 U.S.C. § 112, second paragraph. *See* M.P.E.P. § 2173.04.

The Office Action alleges that the phrase "preparing a solution of nateglinide in ethanol" in claim 6 is indefinite because it is not clear what is the polymorph required. It is well within the knowledge of one of skill in the art that both crystalline and amorphous forms may be used for preparation of a solution because a solid in solution has no crystalline structure. The specification states that "with crystallization processes, the crystalline form of the starting material does not usually affect the final result." *Application*, p. 21, ll. 10-11. The same reasoning would apply for the rejection of claims 15, 20, 23 and 29. Applicants also wish to clarify that contrary what was stated in the rejection of claim 20, claim 20 does not recite "preparing a crystalline form of nateglinide" (emphasis added). *See Office Action*, p. 3, l. 9. There is no limitation in claim 20 that the nateglinide be a crystal; amorphous nateglinide may be used as well.

The Office Action alleges that the phrase "a crystalline form of nateglinide in ethanol" in claim 7 is indefinite because it is not clear what is the polymorph required. One of skill in the art understands that the term "crystalline form" refers to solids having a crystalline structure, as opposed to being amorphous. "Polymorphs are different crystalline forms of the same pure substance in which the molecules have different arrangements" (emphases added). *Polymorphism in Pharmaceutical Solids*, 1999, p. 2. Therefore, the skilled artisan can easily recognize that nateglinide of claim 7 encompasses polymorphs, which by definition possess crystalline structures. The same reasoning would apply for the rejection of claims 16, 21, 27 and 29. Because the scope of the subject matter embraced by these claims is clear, breadth is not indefiniteness, and the claims comply with 35 U.S.C. § 112, second paragraph. *See* M.P.E.P. § 2173.04.

The Office Action alleges that the phrase "storing nateglinide Form T for a sufficient time under suitable temperature" in claim 9 is indefinite because it is unclear

what the time or temperature is. Claim 9 has been amended to clarify that Form T is stored until transition to Form E occurs. When claim 9 is read in light of the specification, the time and temperature for storing Form T until Form E is formed becomes apparent. The specification discloses that "storage at room temperature and pressure may also cause a transition of one form to another." *Application*, p. 14, l. 31-32. An example of the transformation of Form T to Form E is provided in Table III. *Application*, p. 13, Table III. With an example of the storage temperature and polymorphic form of the starting material, one of ordinary skill in the art would know to increase or decrease the temperature within an appropriate range in order to obtain Form E. Knowing the range of suitable temperature to store Form T, the skilled artisan would also be able to determine the storage time for transforming Form T into Form E. Therefore, claim 9 does not need to recite in detail the specific temperature and storage time, since these factors are presumed to be within the level of one of skill in the art.

The Office Action alleges that the phrase "crystalline fomr or claim 18" in claim 19 has no antecedent basis because there is no "crystalline fomr" in claim 18. Claim 19 has been amended to recite "crystalline form," and antecedent basis is now found in claim 18. Applicants therefore respectfully submit that the ground for rejection has been rendered moot, and should be withdrawn.

Claim rejections - 35 U.S.C. § 103

Claims 1-3, 12-14, 17-19, 24-26, 30-33, 36-38 and 41-55 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Sumikawa et al., U.S. Pat. No. 5,463,116 ("the '116 patent"), Sumikawa et al., U.S. Pat. No. 5,488,150 ("the '150 patent"), or Gang et al, *Acta Pharmaceutical Sinica*, 36(7), pp. 532-534 (2001). Applicants respectfully traverse.

"A proper analysis under 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 2 U.S.P.Q. 2d (BNA) 1438, 1442 (Fed. Cir. 1991).

The Office Action concedes that "none of the cited references however disclose nateglinide polymorphs designated as D, F, G, I, O, T, or the methanol, ethanol or isopropanol, n-propanol or n-butanol solvates of nateglinide as described in the instant

claims.” *Office Action*, p. 5, ll. 8-9. The ’116 and ’150 patents teach the preparation of H-type nateglinide crystal. The Gang reference teaches an S-type crystal. One of skill in the art following the teachings of these references would not be motivated to make the nateglinide polymorphs of the invention, nor have a reasonable expectation of success. The search for polymorphic forms is not a predictable science. “No rules exist that allow prediction of whether a compound will exhibit polymorphism.” Byrn, S.R. *Solid-State Chemistry of Drugs* p. 7 (Academic Press 1982) “Until that time [that computer programs are able to predict stable crystal forms] the development scientist is handicapped in attempting to predict how many solid forms of a drug are likely to be found. Brittain, H.G., *Polymorphism in Pharmaceutical Solids* p. 185 (Marcel Dekker 1999). Although general techniques for preparing polymorphic forms are known, there is no accurate way even to determine that a particular isolation technique will produce an amorphous or crystalline form. Because of the unpredictability in the field of polymorphism, existence of one polymorph has little bearing on the presence of another polymorph. Therefore, one of skill in the art following the teachings to produce the H-type and S-type crystals would not be able to make the nateglinide polymorphs of this invention. Applicants respectfully submit that the general state of the art does not support a *prima facie* case of obviousness under the proper legal standard of § 103 and request that the Examiner traverse the rejection.

Objected claims

For the reasons stated above, the currently rejected claims are now in condition for allowance. Therefore, Applicants respectfully submit that the objection to dependent claims 5, 8, 22, 28, 35 and 40 be withdrawn and the claims be allowed.

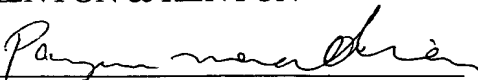
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Applicants would like to interview this application before issuance of subsequent action by the Examiner in order to expedite the prosecution of this point. Please charge any fees required to Kenyon & Kenyon, LLP Deposit Account No. 11-0600.

Respectfully submitted,

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